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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,645	08/01/2003	Linda B. Couto	51271/35:1	5318

24536 7590 07/19/2006

GENZYME CORPORATION
LEGAL DEPARTMENT
15 PLEASANT ST CONNECTOR
FRAMINGHAM, MA 01701-9322

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,645	COUTO ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/14/03;10/2/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Non-Final Rejection

Claims 1-11 are pending.

The sequence listing filed on 6/9/06 is acknowledged. However, there is a problem with the CRF. See attached Notice to Comply.

Election/Restrictions

Applicant's election without traverse of species TTR gene promoter in the reply filed on 6/9/06 is acknowledged.

Claim 4 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/9/06.

Priority

The status of parent applications (09/470,618, 09/364,862) needs updated.

Drawings

The drawings were received on 6/9/06. These drawings are accepted.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "said tissue specific promoter" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The limitation "pharmaceutical composition" in instant claim 1 and claims dependent therefrom does not have patentable weight over the product taught in the prior art. See MPEP 2111.02.

Claims 1-3, 6, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Snyder et al. (US 2002/0155580, cited on an IDS). Snyder teaches a virus particle comprising a recombinant AAV vector comprising a promoter operably linked to a polynucleotide encoding a polypeptide comprising the factor VIII 90kD heavy and light chain with the B-domain deleted (pages 5-12). Snyder teaches that the AAV lacks AAV rep and cap gene (pages 10-11). The

promoter in the vector can be tissue specific for the liver. Snyder further teaches preparing the virus particle in a pharmaceutical excipient (page 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snyder et al. (US 2002/0155580, cited on an IDS) taken with Simonet (US Patent No. 6,268,212, cited on an IDS). Snyder teaches a virus particle comprising a recombinant AAV vector comprising a promoter operably linked to a polynucleotide encoding a polypeptide comprising the factor VIII 90kD heavy and light chain with the B-domain deleted (pages 5-12). Snyder teaches that the promoter can be tissue specific for the liver (page 4). Snyder further teaches that one of ordinary skill in the art will appreciate that a tissue-specific promoter for use in the AAV vector may be selected from any of the known liver-specific promoters (page 4). However, Snyder does not specifically teach a composition comprising a recombinant AAV virion comprising a nucleotide sequence encoding a B-domain deleted human Factor VIII protein operably linked to a liver specific promoter, wherein the liver-specific promoter is the transthyretin (TTR) gene promoter.

However, at the time the invention was made, tissue specific promoter, specifically liver-specific promoters (e.g. TTR) were well known in the art for use in enhancing liver expression of a transgene using a vector as exemplified by Simonet. Simonet teaches several liver-specific promoters (e.g. TTR) that could be used in producing a vector comprising a transgene operably linked to a liver-specific promoter (column 3, line 64-column 4, line 12 and abstract).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention made to combine the teaching of Snyder and Simonet to make a composition comprising a recombinant AAV comprising a nucleotide sequence encoding a B-domain deleted human Factor VIII protein operably linked to a liver specific promoter TTR. One of ordinary skill in the art would have motivated to make the claimed composition because factor VIII is

expressed in the liver and the promoter TTR used to increase gene expression of a vector in the liver.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 6, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snyder et al. (US 2002/0155580) taken with Almstedt et al. (WO 91/09122, cited on an IDS). Snyder teaches a virus particle comprising a recombinant AAV vector comprising a promoter operably linked to a polynucleotide encoding a polypeptide comprising the factor VIII 90kD heavy and light chain with B-domain deleted (pages 5-12). Snyder teaches that in order to improve expression efficiency of Factor VIII, the Factor VIII cDNA was modified lacking most of the B domain (page 2). However, Snyder does not specifically teach a composition comprising a recombinant AAV virion comprising a nucleotide sequence encoding a functional Factor VIII, wherein the nucleotide sequence encodes a heavy and a light chain of Factor VIII with the B domain deleted, and wherein said light chain and heavy chain of Factor VIII are operably linked to a junction having SEQ ID NO: 15.

However, at the time the invention was made, a recombinant factor VIIII protein comprising a first DNA segment coding for the 90kDa chain and a second DNA segment coding for the 80kDa chain of human factor VIII, wherein the segments were interconnected by a linker DNA segment coding for a linker peptide of 4 to about 100 amino acid residues (having SEQ ID NO: 15 of the instant claims) was well known in the art as exemplified by Almstedt (abstract). Almstedt further teaches that the DNA sequence can be expressed in recombinant expression

vectors (abstract). In addition, Almstedt teaches that the smallest active form (one heavy chain and one light chain) with a molecular weight of 170kDa could be activated by thrombin to the same extent as the high molecular weight forms and there was an indication that that smaller form has a 50% longer survival time compared to the higher molecular form (page 4).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention made to combine the teaching of Snyder and Almstedt to make a composition comprising a recombinant AAV virion comprising a nucleotide sequence encoding a B-domain deleted Factor VIII protein, and wherein said nucleotide sequence further encodes a junction (SEQ ID NO: 15) that operably links said heavy and light chain of Factor VIII. One of ordinary skill in the art would have motivated to make the composition because Almstedt teaches that the smaller form of Factor VIII comprising both chains has a 50% longer *in vivo* survival time compared to the higher molecular forms of Factor VIII.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 6-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,200,560. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim from the instant application and the claims from '560 are both directed a recombinant adeno-associated virus comprising a nucleotide sequence encoding a Factor VIII protein operably linked to a promoter.

The claims from '560 do not specifically recite a nucleotide sequence encoding a Factor VIII lacking at least a portion of the B domain. However, in view of the definition of Factor VIII in the specification of '560, the claims of '560 read on the instant claim because the specification teaches that Factor VIII is lacking a B domain (Figure 3). See MPEP 804 which recites that those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent (In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)).

Claims 1-3 and 6-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,221,349. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim from the instant application and the claims from '349 are both directed to a

recombinant adeno-associated virus comprising a nucleotide sequence encoding a Factor VIII protein operably linked to a promoter.

The claims from '349 do not specifically recite a nucleotide sequence encoding a Factor VIII lacking at least a portion of the B domain. However, in view of the definition of Factor VIII in the specification of '349, the claims of '349 read on the instant claim because the specification teaches that Factor VIII is lacking a B domain (Figure 3). See MPEP 804 which recites that those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent (In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)).

Claims 1-3 and 6-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 10/293,400. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims embrace a pharmaceutical composition comprising recombinant adeno-associated virus virions comprising a nucleotide sequence encoding a Factor VIII protein lacking at least a portion of the B domain and the nucleotide sequence operably linked to expression control elements. Both set of claims recite using SEQ ID NO: 13 and 14 (which are 100% identical to SEQ ID NO: 13 and 14 of the instant claims).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

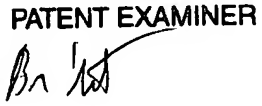
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman
Patent Examiner, Group 1635

BRIAN WHITEMAN
PATENT EXAMINER



Notice to Comply	Application No. 10/632,645	Applicant(s) COUTO et al.	
	Examiner B. Whiteman	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See Raw sequence listing error report.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

B. Whiteman

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/632,645A
Source: FW16
Date Processed by STIC: 6/14/06

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO **REDUCE** ERRORED SEQUENCE LISTINGS, **PLEASE** USE THE **CHECKER VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<**http://www.uspto.gov/ebc/efs/downloads/documents.htm**>, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

IFW16

RAW SEQUENCE LISTING DATE: 06/14/2006
PATENT APPLICATION: US/10/632,645A TIME: 09:53:30

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4 Colosi, Peter B.
5 Qian, Xiabong
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8 VIII
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12 <140> CURRENT APPLICATION NUMBER: US 10/632,645A
13 <141> CURRENT FILING DATE: 2003-08-01
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18 <150> PRIOR APPLICATION NUMBER: US 09/470,618
19 <151> PRIOR FILING DATE: 1999-12-22
21 <150> PRIOR APPLICATION NUMBER: US 09/634,862
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27 <150> PRIOR APPLICATION NUMBER: US 60/104,994
28 <151> PRIOR FILING DATE: 1998-10-20
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3,6

Does Not Comply
Corrected Diskette Needed

RAW SEQUENCE LISTING DATE: 06/14/2006
PATENT APPLICATION: US/10/632,645A TIME: 09:53:30

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RAW SEQUENCE LISTING DATE: 06/14/2006
PATENT APPLICATION: US/10/632,645A TIME: 09:53:30

Input Set : F:\1011CON1.2.ST25.txt
Output Set: N:\CRF4\06142006\J632645A.raw

142 <223> OTHER INFORMATION: PCR fragment EG3
144 <400> SEQUENCE: 9
145 agggaatgtt tgttcttaaa taccatccag ggaatgtttg ttcttaaata ccatccaggg 60
147 aatgtttgtt cttaaatacc atctacagtt attggttaaa gaagtatatt agagcgagtc 120
149 tttctgcaca cagatcacct ttcc 144
152 <210> SEQ ID NO: 10
153 <211> LENGTH: 59
154 <212> TYPE: DNA
155 <213> ORGANISM: Artificial Sequence
157 <220> FEATURE:
158 <223> OTHER INFORMATION: Oligonucleotide SPA.S
160 <400> SEQUENCE: 10
161 tcgagaataa aagatcagag ctctagagat ctgtgtgttg gttttttgtg tgcggccgc 59
164 <210> SEQ ID NO: 11
165 <211> LENGTH: 59 Artificial
166 <212> TYPE: DNA
C--> 167 <213> ORGANISM: Artiificial Sequence
W--> 169 <220> FEATURE:
W--> 169 <223> OTHER INFORMATION:
W--> 169 <400> 11
170 tcgagcggcc gcacacaaaa aaccaacaca cagatctcta gagctctgat cttttattc 59
173 <210> SEQ ID NO: 12
174 <211> LENGTH: 63
175 <212> TYPE: DNA
176 <213> ORGANISM: Artificial Sequence
178 <220> FEATURE:
179 <223> OTHER INFORMATION: PCR fragment SPA
181 <400> SEQUENCE: 12
182 tcgagaataa aagatcagag ctctagagat ctgtgtgttg gttttttgtg tgcggccgct 60
184 cga 63
187 <210> SEQ ID NO: 13
188 <211> LENGTH: 11933
189 <212> TYPE: DNA
190 <213> ORGANISM: Artificial Sequence
192 <220> FEATURE:
193 <223> OTHER INFORMATION: Vector from ITR to ITR
195 <400> SEQUENCE: 13
196 cagctgcgcg ctcgctcgct cactgaggcc gcccgggcaa agcccgggcg tcgggcgacc 60
198 tttggtcgcc cggcctcagt gagcgagcga gcgcgcagag agggagtggc caactccatc 120
200 actaggggtt cctgcggccg cccagggaat gtttgttctt aaataccatc cagggaatgt 180
202 ttgttcttaa ataccatcca gggaatgttt gttcttaaat accatctaca gttattggtt 240
204 aaagaagtat attagagcga gtctttctgc acacagatca cctttccggg tgccgccccc 300
206 aggcaggtaa gtgccgtgtg tggttcccgc gggcctggcc tctttacggg ttatggcccc 360
208 tgcgtgcctt gaattactga cactgacatc cacttttttct ttttctccac aggtatcgat 420
210 tccaccatgc aaatagagct ctccacctgc ttctttctgt gccttttgcg attctgcttt 480
212 agtgccacca gaagatacta cctgggtgca gtggaactgt catgggacta tatgcaaagt 540
214 gatctcggtg agctgcctgt ggacgcaaga tttcctccta gagtgccaaa atcttttcca 600
216 ttcaacacct cagtcgtgta caaaaagact ctgtttgtag aattcacgga tcacctttttc 660
218 aacatcgcta agccaaggcc accctggatg ggtctgctag gtcctaccat ccaggctgag 720

see p. 6 for error explanation

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220 gtttatgata cagtggtcat tacacttaag aacatggctt cccatcctgt cagtcttcat 780
222 gctgttggtg tatcctactg gaaagcttct gagggagctg aatatgatga tcagaccagt 840
224 caaagggaga aagaagatga taaagtcttc cctggtggaa gccatacata tgtctggcag 900
226 gtcctgaaag agaatggtcc aatggcctct gacccactgt gccttaccta ctcatatctt 960
228 tctcatgtgg acctggtaaa agacttgaat tcaggcctca ttggagccct actagtatgt 1020
230 agagaaggga gtctggccaa ggaaaagaca cagaccttgc acaaatttat actacttttt 1080
232 gctgtatttg atgaagggaa aagttggcac tcagaaacaa agaactcctt gatgcaggat 1140
234 agggatgctg catctgctcg ggcctggcct aaaatgcaca cagtcaatgg ttatgtaaac 1200
236 aggtctctgc caggtctgat tggatgccac aggaaatcag tctattggca tgtgattgga 1260
238 atgggcacca ctcctgaagt gcactcaata ttcctcgaag gtcacacatt tcttgtgagg 1320
240 aaccatcgcc aggcgtcctt ggaaatctcg ccaataactt tccttactgc tcaaacactc 1380
242 ttgatggacc ttggacagtt tctactgttt tgtcatatct cttcccacca acatgatggc 1440
244 atggaagctt atgtcaaagt agacagctgt ccagaggaac cccaactacg aatgaaaaat 1500
246 aatgaagaag cggaagacta tgatgatgat cttactgatt ctgaaatgga tgtggtcagg 1560
248 tttgatgatg acaactctcc ttcctttatc caaattcgct cagttgccaa gaagcatcct 1620
250 aaaacttggg tacattacat tgctgctgaa gaggaggact gggactatgc tcccttagtc 1680
252 ctcgcccccg atgacagaag ttataaaagt caatatttga acaatggccc tcagcggatt 1740
254 ggtaggaagt acaaaaaagt ccgatttatg gcatacacag atgaaacctt taagactcgt 1800
256 gaagctattc agcatgaatc aggaatcttg ggacctttac tttatgggga agttggagac 1860
258 acactgttga ttatatttaa gaatcaagca agcagaccat ataacatcta ccctcacgga 1920
260 atcactgatg tccgtccttt gtattcaagg agattaccaa aaggtgtaaa acatttgaag 1980
262 gattttccaa ttctgccagg agaaatattc aaatataaat ggacagtgac tgtagaagat 2040
264 gggccaacta aatcagatcc tcggtgcctg acccgctatt actctagttt cgttaatatg 2100
266 gagagagatc tagcttcagg actcattggc cctctcctca tctgctacaa agaatctgta 2160
268 gatcaaagag gaaaccagat aatgtcagac aagaggaatg tcatcctgtt ttctgtattt 2220
270 gatgagaacc gaagctggta cctcacagag aatatacaac gctttctccc caatccagct 2280
272 ggagtgcagc ttgaggatcc agagttccaa gcctccaaca tcatgcacag catcaatggc 2340
274 tatgtttttg atagtttgca gttgtcagtt tgtttgcatg aggtggcata ctggtacatt 2400
276 ctaagcattg gagcacagac tgacttcctt tctgtcttct tctctggata taccttcaaa 2460
278 cacaaaatgg tctatgaaga cacactcacc ctattcccat tctcaggaga aactgtcttc 2520
280 atgtcgatgg aaaacccagg tctatggatt ctggggtgcc acaactcaga ctttcggaac 2580
282 agaggcatga ccgccttact gaaggtttct agttgtgaca agaacactgg tgattattac 2640
284 gaggacagtt atgaagatat ttcagcatac ttgctgagta aaaacaatgc cattgaacca 2700
286 agaagcttcg aaataactcg tactactctt cagtcagatc aagaggaaat tgactatgat 2760
288 gataccatat cagttgaaat gaagaaggaa gattttgaca tttatgatga ggatgaaaat 2820
290 cagagccccc gcagctttca aaagaaaaca cgacactatt ttattgctgc agtggagagg 2880
292 ctctgggatt atgggatgag tagctcccca catgttctaa gaaacagggc tcagagtggc 2940
294 agtgtccctc agttcaagaa agttgttttc caggaattta ctgatggctc ctttactcag 3000
296 cccttatacc gtggagaact aaatgaacat ttgggactcc tggggccata tataagagca 3060
298 gaagttgaag ataatatcat ggtaactttc agaaatcagg cctctcgtcc ctattccttc 3120
300 tattctagcc ttatttctta tgaggaagat cagaggcaag gagcagaacc tagaaaaaac 3180
302 tttgtcaagc ctaatgaaac caaaacttac ttttggaaag tgcaacatca tatggcaccc 3240
304 actaaagatg agtttgactg caaagcctgg gcttatttct ctgatgttga cctggaaaaa 3300
306 gatgtgcact caggcctgat tggacccctt ctggtctgcc acactaacac actgaaccct 3360
308 gctcatggga gacaagtgac agtacaggaa tttgctctgt ttttcaccat ctttgatgag 3420
310 accaaaagct ggtacttcac tgaaaatatg gaaagaaact gcagggctcc ctgcaatatc 3480
312 cagatggaag atcccacttt taaagagaat tatcgcttcc atgcaatcaa tggctacata 3540
314 atggatacac tacctggctt agtaatggct caggatcaaa ggattcgatg gtatctgctc 3600
316 agcatgggca gcaatgaaaa catccattct attcatttca gtggacatgt gttcactgta 3660

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Input Set : F:\1011CON1.2.ST25.txt
Output Set: N:\CRF4\06142006\J632645A.raw

318 cgaaaaaaag aggagtataa aatggcactg tacaatctct atccaggtgt ttttgagaca 3720
320 gtggaaatgt taccatccaa agctggaatt tggcgggtgg aatgccttat tggcgagcat 3780
322 ctacatgctg ggatgagcac acttttctg gtgtacagca ataagtgtca gactcccctg 3840
324 ggaatggctt ctggacacat tagagatttt cagattacag cttcaggaca atatggacag 3900
326 tgggccccaa agctggccag acttcattat tccggatcaa tcaatgcctg gagcaccaag 3960
328 gagccctttt cttggatcaa ggtggatctg ttggcaccaa tgattattca cggcatcaag 4020
330 acccagggtg cccgtcagaa gttctccagc ctctacatct ctcagtttat catcatgtat 4080
332 agtcttgatg ggaagaagtg gcagacttat cgaggaaatt ccactggaac cttaatggtc 4140
334 ttctttggca atgtggattc atctgggata aaacacaata tttttaaccc tccaattatt 4200
336 gctcgataca tccgtttgca cccaactcat tatagcattc gcagcactct tcgcatggag 4260
338 ttgatgggct gtgatttaaa tagttgcagc atgccattgg gaatggagag taaagcaata 4320
340 tcagatgcac agattactgc ttcatcctac tttaccaata tgtttgccac ctggtctcct 4380
342 tcaaaagctc gacttcacct ccaagggagg agtaatgcct ggagacctca ggtgaataat 4440
344 ccaaaagagt ggctgcaagt ggacttccag aagacaatga aagtcacagg agtaactact 4500
346 cagggagtaa aatctctgct taccagcatg tatgtgaagg agttcctcat ctccagcagt 4560
348 caagatggcc atcagtggac tctctttttt cagaatggca aagtaaaggt ttttcaggga 4620
350 aatcaagact ccttcacacc tgtggtgaac tctctagacc caccgttact gactcgctac 4680
352 cttcgaattc acccccagag ttgggtgcac cagattgccc tgaggatgga ggttctgggc 4740
354 tgcgaggcac aggacctcta ctgactcgag aataaaagat cagagctcta gagatctgtg 4800
356 tgttggtttt ttgtgtgcgg ccgcaggaac ccctagtgat ggagttggcc actccctctc 4860
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362 gccagcaaaa ggccaggaac cgtaaaaagg ccgcgttgct ggcgtttttc cataggctcc 5040
364 gccccccctga cgagcatcac aaaaatcgac gctcaagtca gaggtggcga aacccgacag 5100
366 gactataaag ataccaggcg tttcccccctg gaagctccct cgtgcgctct cctgttccga 5160
368 ccctgccgct taccggatac ctgtccgcct ttctcccttc gggaagcgtg gcgctttctc 5220
370 atagctcacg ctgtaggtat ctcagttcgg tgtaggtcgt tcgctccaag ctgggctgtg 5280
372 tgcacgaacc ccccgttcag cccgaccgct gcgccttatc cggtaactat cgtcttgagt 5340
374 ccaacccggt aagacacgac ttatcgccac tggcagcagc cactggtaac aggattagca 5400
376 gagcgaggta tgtaggcggt gctacagagt tcttgaagtg gtggcctaac tacggctaca 5460
378 ctagaaggac agtatttggt atctgcgctc tgctgaagcc agttaccttc ggaaaaagag 5520
380 ttggtagctc ttgatccggc aaacaaacca ccgctggtag cggtggtttt tttgtttgca 5580
382 agcagcagat tacgcgcaga aaaaaaggat ctcaagaaga tcctttgatc ttttctacgg 5640
384 ggtctgacgc tcagtggaac gaaaactcac gttaagggat tttggtcatg agattatcaa 5700
386 aaaggatctt cacctagatc cttttaaatt aaaaatgaag ttttaaatca atctaaagta 5760
388 tatatgagta aacttggtct gacagttacc aatgcttaat cagtgaggca cctatctcag 5820
390 cgatctgtct atttcgttca tccatagttg cctgactccc cgtcgtgtag ataactacga 5880
392 tacgggaggg cttaccatct ggccccagtg ctgcaatgat accgcgagac ccacgctcac 5940
394 cggctccaga tttatcagca ataaaccagc cagccggaag ggccgagcgc agaagtggtc 6000
396 ctgcaacttt atccgcctcc atccagtcta ttaattgttg ccgggaagct agagtaagta 6060
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408 aatagtgtat gcggcgaccg agttgctctt gcccggcgtc aatacgggat aataccgcgc 6420
410 cacatagcag aactttaaaa gtgctcatca ttggaaaacg ttcttcgggg cgaaaactct 6480
412 caaggatctt accgctgttg agatccagtt cgatgtaacc cactcgtgca cccaactgat 6540
414 cttcagcatc ttttactttc accagcgttt ctgggtgagc aaaaacagga aggcaaaatg 6600

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 06/14/2006
PATENT APPLICATION: US/10/632,645A TIME: 09:53:31

Input Set : F:\1011CON1.2.ST25.txt
Output Set: N:\CRF4\06142006\J632645A.raw

error explanation

Use of <220> Feature(NEW RULES):
Sequence(s) __ are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence" or"Unknown". Please explain source of genetic material in <220> to <223> section (See "Federal Register," 6/01/98, Vol. 63, No. 104,pp.29631-32) (Sec.1.823 of new Rules)

Seq#:11

VERIFICATION SUMMARY DATE: 06/14/2006
PATENT APPLICATION: US/10/632,645A TIME: 09:53:31

Input Set : F:\1011CON1.2.ST25.txt
Output Set: N:\CRF4\06142006\J632645A.raw

L:167 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:11
L:169 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:11, <213> ORGANISM:Artificial Sequence
L:169 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:11, <213> ORGANISM:Artificial Sequence
L:169 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:11,Line#:169